Since 1983
EPITHEORESE KLINIKES FARMAKOLOGIAS KAI FARMAKOKINETIKES | 42(Sup1): 93-100 (2024)

Received: 05 February 2024 | **Accepted**: 11 May 2024 | **Published**: 27 December 2024

Open Access | RESEARCH

The efficacy of *Salvia officinalis* mouthwash extract on gingivitis and its acceptance by pediatric patients: an *in vivo* comparative study

Samah F. Mohamed-Ali[1], Ahmed A. Jasim[2,*], Mafaz M. Mohsin[3]

[1]Department of Pediatric, Orthodontic & Preventive dentistry, College of Dentistry, Mustansiriyah University,Baghdad, Iraq
[2]Department of Conservative Dentistry, College of Dentistry, Mustansiriyah University, Baghdad, Iraq
[3]Department of Pediatric Orthodontic & Preventive dentistry, College of Dentistry, Al-Bayan University, Baghdad, Iraq

***Corresponding author:** Ahmed A. Jasim, Department of Conservative Dentistry College of Dentistry, Mustansiriyah University, Baghdad, Iraq; Tel.: +964-7713854901; e-mail: ahmedajasim88@uomustansiriyah.edu.iq

ABSTRACT

Background: Children are more prone to develop gingivitis as a result of poor brushing and flossing proficiency, a lack of dedication to maintaining excellent oral hygiene, morphological variance in deciduous teeth, and a diet that encourages the growth of pathogenic oral bacteria. *Aim*: The aim of this study is to compare the therapeutic effect of a *Salvia officinalis* (Common Sage) extract mouth rinse related to that of Chlorhexidine mouth rinse, as well as the pediatric patient's tolerance to their taste. *Methodology:* In this study 48 patients aged between (8-10) years divided into 3 groups each with 16 patients one treated using Sage mouthwash the second treated with Chlorhexidine mouthwash (0.12%) (Positive control) third group treated with distilled water (negative control). One way ANOVA with Tukey's Honest Significant Difference HSD test were used for data assessment. *Results:* Significant differences were found among tested groups ($P<0.05$) regarding gingival index and acceptance of the mouth washes being evaluated. Chlorhexidine has superior efficacy compared to Sage in treating gingivitis, however Sage should better acceptance from patients. *Conclusion:* Herbal mouthwashes made from *Salvia officinalis* have a lot of potential for treating and preventing periodontal disease in young children, and they have less side effects than conventional mouthwashes.

KEYWORDS

herbal mouthwash, chlorhexidine, *Salvia officinalis,* gingivitis, common sage

How to cite this article: Mohamed-Ali S. F., Jasim A. A., Mohsin M. M.: The efficacy of *Salvia officinalis* mouthwash extract on gingivitis and its acceptance by pediatric patients: an *in vivo* comparative study. *Epitheorese Klin. Farmakol. Farmakokinet.* 42(Sup1): 93-100 (2024). DOI: 10.61873/EIBC9338

Publisher note: PHARMAKON-Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. INTRODUCTION

Bacterial plaque accumulation on the surfaces of teeth throughout early childhood is the foremost source of periodontal disease, which destroys the gingiva and the bone structures that support the teeth. Additionally, periodontal disease, particularly gingivitis, is more common in children [1].

Low awareness of the importance of practicing good oral hygiene combined with anatomical differences between children's and adults' periodontium's, including the width of the attached gingiva

and the existence of spaces between teeth that are ideal for the growth of bacteria [2].

Dental caries, gingivitis, periodontal disease, bad breath, and other dental conditions can be prevented by practicing oral hygiene and maintaining a clean mouth. The main ways to reduce plaque are with mechanical oral hygiene procedures including tooth brushing, interdental brushing, and dental flossing; nevertheless, studies based on populations and clinical experience suggest that many people do not use these methods correctly. [3]

Younger children find it difficult to remove plaque, thus using antiplaque mouthwash with an antibacterial activity is necessary since it is less demanding than employing mechanical methods [4,5]. Chlorhexidine mouthwash has been recognized as the ultimate benchmark against which the efficiency of other antiplaque therapies is assessed [6,7].

Long-term use of Chlorhexidine mouthwash may result in a variety of undesirable consequences, including foul taste and tooth discoloration, which has led to the quest for safer alternatives to mouthwash that young children may use for extended periods of time without experiencing negative effects [8].

There are two strengths of chlorhexidine mouthwash: 0.2% and 0.12% [9]. The 0.12% chlorhexidine utilized during this study not only had the same therapeutic impact as a 0.2% solution, but it also lessened the unpleasant taste and stains encountered from employing chlorhexidine, thereby rendering it more suitable for children [10,11].

For countless epochs, plants have long been used as a source of medicinal compounds. Numerous bioactive compounds are alleged to be accountable for these physiognomies. Besides, Herbal products are inexpensive and have few adverse effects [12].

Common Sage, also known as *Salvia officinalis, is routinely* used in traditional medicine, cosmetics, and food flavoring. *Salvia officinalis* is a widespread fragrant herb that is also well recognized for its antibacterial capabilities [13,14,15]. These qualities have been attributed to diverse spectrum of phytochemicals of *S. officinalis* which contains Phenolic compounds, polyacetylenes, steroids, terpenoids, alkaloids, polysaccharides, fatty acids, glyosidic derivatives, and essential oils.

Salvia officinalis is frequently used as herbal medicine for oral inflammation and ulcers such as gingivitis, as well as laryngitis [16]. The aim of this study is to evaluate the clinical effect of a *Salvia officinalis* extract mouth rinse in comparison to that of Chlorhexidine mouth rinse, as well as the pediatric patient's tolerance to the mouthwash taste.

2. METHODOLOGY

2.1. Ethics approval of research

This study was designed to be experimental and conducted at the clinical facilities of Mustansiriyah University. The approval for performing study was obtained from human research ethical committee in the Mustansiriyah University College of Dentistry's (REC reference: REC141 clinical trial was given the number: MUPED02 in 1/9/2022). The study was carried out in accordance with the Declaration of Helsinki.

2.2. Study population

The study took place at Mustansiriyah University College of Dentistry's pediatric clinic in Baghdad, Iraq, over a six-month period (September 2022-February 2023). A total of 48 patients (30 boys, 18 girls) aged between (8-10) years were assessed in this study.

The parents of potential children's candidates were initially briefed about the study's purpose, the treatment which were to be provided and the period of time for the study. Later, both verbal and written informed consent were obtained and signed by subject's guardians who were willingly to allow their children to participate. Patient's guardians' who did not provide consent were excluded from the study.

2.3. Clinical study design

In this study the patients were omitted based on criteria of absence of long-term prescription drugs usage, current antibiotic usage, presence of systemic illness, allergies, Patients shouldn't have used mouthwashes or experienced pathologic changes to their oral mucosa throughout the preceding thirty days earlier to date of participation in this study.

The requirements for inclusion were a gingival index (GI) of 1.1-2 evaluated clinically by two dentists specialized in pediatric dentistry with clinical experience of 10 years in accordance with standards described by Leo and Silness (1964) [17,18].

The participants were picked at random from patients seeking treatment at the Department of Pediatric Dentistry clinic, and were and allocated to one of three therapy groups of this study.

2.4 Herbal extract preparation

The process of fabrication of the herbal extract was performed in the Microbiology laboratories of

the Mustansiriyah University College of Dentistry. Starting with 5 Kg. of dried sage's leaves were bought at the apothecary.

The leaves were pulverized into powder then immersed in 50 L of 70% Ethanol and frequently agitated for one week. The mixture was purified with a double linen fabric filter and then heated in a multi-function rotary evaporator at 60ºC for 1 week until very viscous extract was obtained which was kept in a hermetically sealed flask and refrigerated until usage. 0.5ml of extract was diluted to 100 ml of distilled water [19].

2.5 Patients group distribution

Participants were split up into three groups, Group I (n = 16): gurgled with Sage mouthwash, Group II (n = 16): rinsed with Chlorhexidine mouthwash (0.12%) (Positive control) and Group III (n = 16): were given distilled water (negative control) gingival index was computed bestowing to the scheme specified by Loe and Silness afore the treatment (0 reading), after one week of mouth rinsing (7 days) and after two weeks of treatment (14 days) [20].

2.6 Study protocol

All solutions of mouthwashes were prepared in identical flasks with the matching hue to discount bias. The flasks were coded and at the conclusion of the study the decoding was done. Children were taught to rinse their mouth with 10 ml of prepared mouthwash in their respective groups for a period of 1 minute twice daily. The period between these two rinsing was approximately 12 hours.

This schedule was consistent with the standardized protocol of Chlorhexidine mouthwash, which must be used at 12-hour intervals since it has been found to reduce salivary bacterial counts for more than 12 hours [21].

The children were advised not to eat or rinse their mouth for the next 30 min. to linger the retention of Chlorhexidine in the oral cavity as is stated by Walton and Thompson [22].

After two weeks of using the mouth washes, patient acceptance was recorded by asking each child about their level of rejection or acceptance to the mouthwash provided and recorded in a scale range of (0 score) for reluctant to use, (1 score) for moderate acceptance and (2 score) for good willing to use with no complaint.

2.7. Statistical analysis

Data assembled was recorded in a specially prepared sheet. It comprised patient identification and clinical examination data on gingival index (GI) values. Later, all data were entered into Microsoft Excel spreadsheet (Microsoft, USA). To perform the necessary data tabulation and coding.

The hypothesis was tested using the ANOVA test, followed by multiple comparisons using the Tukey HSD (honestly significant difference) post-hoc test. For comparing means across research groups. All statistical analyses were conducted using version 21 of The Statistical Package for the Social Sciences (SPSS IBM) Chicago, Illinois, United States).

3. RESULTS

3.1 Sample attrition

There was no sample attrition in any of the three groups.

3.2 Gingivitis score

Table1 represents descriptive statistics where the mean of gingival scores for the Group I, II, and III are depicted. ANOVA was used to analyze the reduction in gingivitis in the three groups.

No statistical differences were observed at the start of treatment in the baseline value. However, in the middle and the end of the study statistical differences were observed. Thus, multiple comparisons through Tukey HSD (honestly significant difference) post hoc test were performed to pinpoint which pairs are with significant differences. There was a significant decrease in the gingivitis in both the chlorhexidine and Sage groups at 7 days and 14 days ($P < 0.05$) Table 2.

The Chlorhexidine group showed maximum decrease as compared to the Sage group. The difference in the decrease in gingivitis between Sage and Chlorhexidine groups was statistically significant at both measuring intervals.

Regarding the agreement and compliance (tastefulness) of patients for the Chlorhexidine, Sage mouth rinses and the water placebo, Table 3. Represents descriptive statistics where the mean of agreement scores for the Group I, II, and III measured at the end of the treatment after 2 weeks are depicted. The most distasteful mouth rinse was the Chlorhexidine followed by the sage and the water placebo.

ANOVA test determined presence of significant differences which was confirmed with Tukey HSD post hoc test Table 4. The water placebo was the least distasteful followed by the sage followed by Chlorhexidine as the most distasteful to the patients.

Table 1. Descriptive statistics of Gingivitis index (GI) for the three study groups of patients being treated of gingivitis, which were measured at the start of the treatment, one week and after 2 weeks of treatment.

		N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Start	Water	16	1.61	0.309	0.077	1.10	2.00
	Sage	16	1.61	0.314	0.078	1.10	2.00
	Chx.	16	1.61	0.309	0.077	1.10	2.00
7 Days	Water	16	1.62	0.308	0.077	1.10	2.00
	Sage	16	1.40	0.270	0.067	1.00	1.80
	Chx.	16	1.17	0.180	0.045	0.70	1.40
14 Days	Water	16	1.59	0.302	0.075	1.10	2.00
	Sage	16	1.25	0.255	0.063	0.90	1.60
	Chx.	16	0.91	0.190	0.047	0.60	1.20

N= number; Std. = Standard; Chx. =Chlorhexidine

Table 2. Gingivitis index (GI) ANOVA and Tukey HSD Post -hoc tests results for the three study groups of patients being treated of gingivitis which were measured at the start of the treatment, one week and after 2 weeks of treatment.

		Sum of squares	DF	Mean square	*F*-value	*P*-value*	Tukey HSD Post -hoc
Start	Between groups	0.000	2	0.000	0.002	0.998	Non-significant
	Within groups	4.359	45	0.097			
7 days	Between groups	1.620	2	0.810	12.070	0.000	Chx>Sage Water = Non-significant
	Within groups	3.020	45	0.067			
14 days	Between groups	3.645	2	1.823	28.347	0.000	Chx>Sage; Water = Non-significant
	Within groups	2.893	45	0.064			

*P<0.05 indicates significant; DF= degrees of freedom; Chx. =Chlorhexidine

Table 3. Descriptive statistics of patient agreement (tastefulness) to 3 mouthwashes being evaluated in this study measured at the end of the study.

	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Water	16	2.00	0.000	0.000	2.00	2.00
Sage	16	1.75	0.447	0.111	1.00	2.00
Chx.	16	1.12	0.806	0.201	0.00	2.00
Total	48	1.62	0.639	0.092	0.00	2.00

N= number; Std. = Standard; Chx. =Chlorhexidine

Table 4. ANOVA and Tukey HSD Post -hoc tests results of patients' agreement to treatments of patient agreement (tastefulness) to 3 mouthwashes being evaluated in this study measured at the end of the study.

	Sum of squares	DF	Mean square	*F*-value	*P*-value*	Tukey HSD Post -hoc
Between groups	6.500	2	3.250	11.471	0.000	Chx. >Sage; Chx. > Water Sage=Water(non-significant)
Within groups	12.750	45	0.283			
Total	19.250	47				

*P<0.05 indicates significant; DF= degrees of freedom; Chx. =Chlorhexidine

4. DISCUSSION

According to numerous researches, Iraq has a substantial prevalence of periodontal disease and dental caries, since basic dental health is not given much importance by most people, especially in rural and underdeveloped areas [23].

For the treatment of oral and dental illnesses, mechanical plaque removal has been the standard approach practiced worldwide. Yet, data illustrate that mechanical cleaning techniques are inadequate [24,25,26].

For more than 50 years, Chlorhexidine has been regarded as the main chemical agent for controlling plaque. Chlorhexidine, nonetheless, has a sum of adversarial consequences [27,28].

The elevated expense of artificial mouthwashes with antiplaque agents caused a shift to traditional medicine as a crucial source of healthcare for 65-80% of the world's population according to the World Health Organization [29,30]. Hence, herbal mouthwashes appear to be potential substitutes to Chlorhexidine based mouthwashes for the daily oral hygiene of patients with gingivitis, particularly for prolonged usage [31].

Natural plant-based Gingivitis therapies seem to be a viable choice. Natural substances in Sage such as Terpenoids, Steroids, Fatty acids, Rusolic acid in Sage and Sage-based remedies may reduce growth and adherence of oral bacteria and diminish cytokines such as Interleukin-6 and Tumor necrosis factor (TNF) that mediate inflammation [32, 33]. Besides, antioxidant attributes of sage based mouthwashes may guard the gingiva against infection and inflammation [34].

The drive behind this study was to determine if Sage mouthwash can successfully lessen gingivitis in children [15].

Numerous studies have revealed that *S. officinalis* has antibacterial assets towards a broad spectrum of bacterial strains. Moreover, Oliveira *et al.* assessed the antibacterial and non-cytotoxic profiles of *S. officinalis* glycolic extract concentrations against *Streptococcus mutans*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Candida* species clinical samples. At 50 mg/mL, this extract kills all strains [35].

Another study on cariogenic bacteria discovered that when mixed with glass-ionomer Cement (GIC), this extract inhibited *S. mutans* and *Lactobacillus casei* [36]. Bajpai and Tripathi (2010) in their study on the antibacterial activities of the essential oils showed that *Salvia officinalis* exhibited bacteriostatic and bactericidal activities against *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis* and *Klebsiella oxytoca* [37].

A meta-analysis by HeCai *et.al*. Comparing the effectiveness of herbal and chlorhexidine mouthwashes on dental plaque revealed no discernible differences between the two types of mouthwashes. The antibacterial, anti-inflammatory, and antioxidant properties of herbal medications make them popular for maintaining good oral hygiene [31].

Though the results of herbal mouthwashes are less efficient than chlorhexidine mouthwash, they can be utilized as a suitable oral prophylactic because they have no negative side effects. Various herbal mouthwashes possess anti-inflammatory, anti-microbial, and anti-oxidant qualities that improve oral hygiene when compared to conventional mouthwashes containing Chlorhexidine [38].

In a research evaluating patients treated with herbal remedies and Chlorhexidine, the bacteria growth was significantly inhibited in both groups, resulting in less plaque and reduced the underlying gingivitis, although Chlorhexidine group had adverse effects such as tongue dryness and feeling of burning there was none displayed by the herbal group [39].

In a different study, patients with moderate-to-severe periodontitis used an herbal mouthwash containing *Salvia officinalis*, which significantly reduced gingival hemorrhage and plaque accumulation when compared to mouthwash containing Chlorhexidine. With comparable effect upon probing depth and clinical attachment level [40].

Similar results were found in another study that examined the protective properties of *Salvia officinalis* essential oil against common mouth infections [41]. Numerous studies showed that the effectiveness of mouthwash containing Chlorhexidine and essential oil of *Salvia officinalis* were equivalent [42]. *S. officinalis* is aromatic with a pleasant scent, and doesn't produce any of the adverse effects of Chlorhexidine, such metallic taste, dry mouth, discolored teeth, or irritation of the oral mucosa, according to studies that have been published. [43]

This study findings validate previous reports on the antibacterial activity of *S. officinalis* and emphasize that a key component of this action is Manool, a Labdane diterpenoid ($C_{20}H_{34}O$) [44, 45, and 46].

The results of this study exhibited that although herbal mouthwash is not as efficient as Chlorhexidine in treating gingivitis, pediatric patients did not like the bitter taste or aftertaste that Chlorhexidine left in their mouths. Since it can be challenging to persuade young children to comply with regimens, this may limit the potential benefits of Chlorhexidine. However, because the *Salvia officinalis*

mouthwash didn't taste unpleasant or leave a foul aftertaste when they rinsed their mouths with this herbal mouth wash, the kids appreciated it. Furthermore, *Salvia officinalis* mouthwash reduced children's gingivitis scores.

5. CONCLUSION

Herbal mouthwashes offer a lot of promise to help treat and prevent periodontal diseases in young children, they have less adverse effects and are more readily accepted by the children than traditional chemical mouthwashes.

ACKNOWLEDGMENTS
The authors would like to express their gratitude to Mustansiriyah and Al-Bayan Universities Colleges of Dentistry and Dr. Apostolos Zarros for their invaluable support in completing this research project.

CONFLICT OF INTEREST STATEMENT
The authors declare no conflicts of interest.

REFERENCES

1. Oh T., Eber R., Wang H.: Periodontal diseases in the child and adolescent. *J. Clin. Periodo*. 29(5): 400–10 (2002).
DOI: 10.1034/j.1600-051x.2002.290504.x

2. Pari A., Ilango P., Subbareddy V., Katamreddy V., Parthasarthy H.: Gingival diseases in childhood–A review. *J. Clin. Diag. Re.* 8(10): ZE01 (2014).
DOI: 10.7860/jcdr/2014/9004.4957

3. Subburaman N., Kumar P. D., Iyer K.: Effectiveness of musical toothbrush on oral debris and gingival bleeding among 6–10-year-old children: A randomized controlled trial. *Ind. J. Den. Res*. 30(2): 196-199 (2019).
DOI: 10.4103/ijdr.ijdr_128_17.

4. MacGregor I. D., Rugg-Gunn A. J.: A survey of toothbrushing sequence in children and young adults. *J. Perio. Res*.14(3): 225-30 (1979).
DOI: 10.1111/j.1600-0765.1979.tb00227.x

5. Barnett M. L.: The role of therapeutic antimicrobial mouthrinses in clinical practice: Control of supragingival plaque and gingivitis. *J. Am. Den. As*. 134: 699-704 (2003).
DOI: 10.14219/jada.archive.2003.0255

6. Jong F. J., Ooi D. J., Teoh S. L.: The effect of oil pulling in comparison with chlorhexidine and other mouthwash interventions in promoting oral health: A systematic review and meta-analysis. *Int. J. Den. Hyg.* 22(1): 78-94 (2024).
DOI: 10.1111/idh.12725

7. Navabi N., Afshari Z., Kamyabi H., Mohammadi M.: Side effects and short effects of using three common mouthwashes on oral health and quality of life: A quasi-experimental study. *Int. J. Den. Hyg*. (2023).
DOI: 10.1111/idh.12761

8. Karamani I., Kalimeri E., Seremidi K., Gkourtsogianni S., Kloukos D.: Chlorhexidine Mouthwash for Gingivitis Control in Orthodontic Patients: A Systematic Review and Meta-Analysis. *Or. H. Prev. Den*. 20(1): 279-94 (2022).
DOI: 10.1002/cre2.417

9. Kolliyavar B., Shettar L., Thakur S.: Chlorhexidine: the gold standard mouth wash. *J.Phar. Bio. Sci*. 6(2) (2016).
DOI: 10.20936/jpbms/160205

10. Segreto V. A., Collins E. M., Beiswanger B. B., De La Rosa M., Isaacs R.L., Lang N.P., Mallatt M. E., Meckel A. H. *et al*.: A comparison of mouthrinses containing two concentrations of chlorhexidine. *J. Perio. Res*. 21: 23-32 (1986).
DOI: 10.1111/j.1600-0765.1986.tb01512.x

11. Addy M.: Chlorhexidine compared with other locally delivered antimicrobials: a short review. *J. Clin. Perio*.13(10): 957-64 (1986).
DOI: 10.1111/j.1600-051x.1986.tb01434.x

12. Schönknecht K., Surdacka A., Rudenko L., Scherer W.: Effectiveness of composed herbal extract in the treatment of gingivitis and oral and pharyngeal mucosa–review of studies. *Wiad Lek*. 74(7): 1737-49 (2021).
DOI: 10.36740/wlek202107131

13. Ghorbani A., Esmaeilizadeh M.: Pharmacological properties of *Salvia officinalis* and its components. *J. Trad. Comp. Med*. 7(4): 433-40 (2017).
DOI: 10.1016/j.jtcme.2016.12.014

14. Petrovska B. B.: Historical review of medicinal plants' usage. *Pharm. Rev*. 6(11): 1 (2012).
DOI: 10.4103/0973-7847.95849

15. Mendes F. S., Garcia L. M., da Silva Moraes T., Casemiro L. A., de Alcantara C. B., Ambrósio S. R., Veneziani R. C., Miranda M. L., Martins C. H.: Antibacterial activity of *salvia officinalis* L. against periodontopathogens: An *in vitro* study. *Anaer. J.* 63: 102194 (2020).
DOI: 10.1016/j.anaerobe.2020.102194

16. Garcia C. S., Menti C., Lambert A. P., Barcellos T., Moura S., Calloni C., Branco C. S., Salvador M., Roesch-Ely M., Henriques J. A.: Pharmacological perspectives from Brazilian *Salvia officinalis* (Lamiaceae): antioxidant, and antitumor in mammalian cells. *A. Acad. Brasi. Ciê*. 88: 281-92 (2016).
DOI: 10.1590/0001-3765201520150344

17. Silness J., Löe H.: Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *A. Od. Scand*. 22(1): 121-35 (1964).
DOI: 10.3109/00016356408993968

18. Löe H., Silness J.: Periodontal disease in pregnancy I. Prevalence and severity. *A. Od. Scand*. 21(6): 533-51 (1963).
DOI: 10.3109/00016356309011240

19. Beheshti-Rouy M., Azarsina M., Rezaie-Soufi L., Alikhani M. Y., Roshanaie G., Komaki S.: The antibacterial effect of sage extract (*Salvia officinalis*) mouthwash against Streptococcus mutans in dental plaque: a randomized clinical trial. Ir. J. Micro. 7(3): 173-7 (2015).

20. Silness J., Löe H.: Periodontal Disease in Pregnancy. 3. Response to Local Treatment. *Acta. Odontol. Scand*. 24(6): 747-59 (1966).
DOI: 10.3109/00016356609028739

21. Moshrefi A.: Chlorhexidine. *J West Soc Periodontol Periodontal Abstr.* 50(1): 5-9 (2002).

22. Gowtham K., Hugar S. M., Hallikerimath S., Mundada M. V., Badakar C., Shah S.V.: Antimicrobial Efficacy of Chlorhexidine and Herbal Mouth Rinse on Salivary *Streptococcus mutans* in Children with Mixed Dentition: A Randomized Crossover Study. *Int. J. Clin. Ped. Den*. 15(1): 99–103 (2022).
DOI: 10.5005/jp-journals-10005-2348

23. Abdulbaqi H. R., Abdulkareem A. A., Alshami M. L., Milward M. R.: The oral health and periodontal diseases awareness and knowledge in the Iraqi population: Online-based survey. *Clin.Exp. Den. Res*. 6(5): 519-28 (2020).
DOI: 10.1002/cre2.304

24. Addy M., Griffiths G., Dummer P., Kingdom A., Shaw W. C.: The distribution of plaque and gingivitis and the influence of toothbrushing hand in a group of South Wales 11–12-year-old children. *J. Clin. Perio*. 14(10): 564-72 (1987).
DOI: 10.1111/j.1600-051x.1987.tb01517

25. De la Rosa M., Johnston D. A., Radike A. W.: Plaque growth and removal with daily toothbrushing. *J. Perio*. 50(12): 661-4 (1979).
DOI: 10.1902/jop.1979.50.12.661

26. Kleinman D., Löe H.: Dental plaque control measures and oral hygiene practices: proceedings from a state-of-the-science workshop. *Ox. Uni. Pr.* (1986).
DOI: 10.1016/0300-5712(87)90080-7

27. Flötra L., Gjermo P. E., Rölla G., Waerhaug J.: Side effects of chlorhexidine mouth washes. *Eu. J Or. Sci*. 79(2): 119-25 (1971).
DOI: 10.1111/j.1600-0722.1971.tb02001.x

28. Jones C. G.: Chlorhexidine: is it still the gold standard? *Periodontol 2000*. 15: 55-62 (1997).
DOI: 10.1111/j.1600-0757.1997.tb00105.x

29. Laelago T., Yohannes T., Lemango F.: Prevalence of herbal medicine use and associated factors among pregnant women attending antenatal care at public health facilities in Hossana Town, Southern Ethiopia: facility based cross sectional study. *Arch. Pub. H*. 74(1): 1-8 (2016).
DOI: 10.1186/s13690-016-0118-z

30. Moran J. M.: Chemical plaque control-prevention for the masses. *Periodontol 2000.* 15: 109-17 (1997)
DOI:10.1111/j.1600-0757.1997.tb00110.x

31. Jenabian N., Moghadamnia A. A., Karami E., Mir A. P. B.: The effect of *Camellia Sinensis* (green tea) mouthwash on plaque-induced gingivitis: a single-blinded randomized controlled clinical trial. *DARU*. 20: 1-6 (2012).
DOI: 10.1186/2008-2231-20-39

32. Gupta D., Bhaskar D. J., Gupta R. K., Karim B., Jain A., Singh R., Karim W.: A randomized controlled clinical trial of *Ocimum sanctum* and chlorhexidine mouthwash on dental plaque and gingival inflammation. *J. Ayur. Int. Med*. 5(2):109 (2014).
DOI:10.4103/0975-9476.131727

33. Radafshar G., Ghotbizadeh M., Saadat F., Mirfarhadi N.: Effects of green tea (*Camellia sinensis*) mouthwash containing 1% tannin on dental plaque and chronic gingivitis: a double-blinded, randomized, controlled trial. *J. Inv. Clin. Den*. 8(1) (2017).
DOI: 10.1111/jicd.12184

34. Asokan S., Emmadi P., Chamundeswari R.: Effect of oil pulling on plaque induced gingivitis: A randomized, controlled, triple-blind study. *Ind. J. Den. Res.* 20(1): 47 (2009).
DOI: 10.4103/0970-9290.49067

35. De Oliveira J. R., Vilela P. G., Almeida R. D., De Oliveira F. E., Carvalho C. A., Camargo S. E., Jorge A. O, de Oliveira L. D.: Antimicrobial activity of noncytotoxic concentrations of *Salvia officinalis* extract against bacterial and fungal species from the oral cavity. *Gen. Den. J.* 67(1): 22-6 (2019).
DOI: 10.1186/1472-6882-13-208

36. Shahriari S., Barekatain M., Shahtalebi M. A., Farhad S. Z.: Evaluation of preventive antibacterial properties of a glass-ionomer cement containing purified powder of *Salvia officinalis*: An *In vitro* Study. *Int. J. Prev. Med*. 10 (2019).
DOI: 10.4103/ijpvm.ijpvm_81_17

37. Longaray Delamare A. P., Moschen-Pistorello I. T., Artico L., Atti-Serafini L., Echeverrigaray S.: Antibacterial activity of the essential oils of *Salvia officinalis* L. and *Salvia triloba* L. cultivated in South Brazil. *F. Chem. J.* 100(2): 603–8 (2007).
DOI: 10.1016/j.foodchem.2005.09.078

38. Parwani S. R., Parwani R. N., Chitnis P. J., Dadlani H. P., Prasad S. V.: Comparative evaluation of anti-plaque efficacy of herbal and 0.2% chlorhexidine gluconate mouthwashina 4-day plaque re-growth study. *J. Ind. Soc. Perio.* 17(1): 72-7 (2013).
DOI: 10.4103/0972-124x.107478

39. Joshi V., Pathan M., Bhat K.: Comparative evaluation of the efficacy of a herbal mouthwash and chlorhexidine

mouthwash on select periodontal pathogens: An *in vitro* and *ex vivo* study. *J. Indian. Soc. Periodontol*. 21(4): 270-275 (2017).
DOI: 10.4103/jisp.jisp_382_16

40. Sparabombe S., Monterubbianesi R., Tosco V., Orilisi G., Hosein A., Ferrante L., *et al*.: Efficacy of an all-natural polyherbal mouthwash in patients with periodontitis: A single-blind randomized controlled trial. *Front. Phy. J*. 10: 632 (2019).
DOI: 10.3389/fphys.2019.00632

41. Haider A. K., Naseem S. B., Iqbal Z., Ashar F., Kaif M. Z., Fayyaz M.T.: Comparison of Antibacterial Properties of *Salvia Officinalis* with Commercially Available Mouth-Rinse. Pakistan *J. Med. H. Sci.* 17(1): 372–4 (2023).
DOI: 10.53350/pjmhs2023171372

42. Khobragade V. R., Vishwakarma P., Dodamani A. S., Kshirsagar M. M., Raut S. N., Deokar R. N.: Herbal Mouth-wash for the Management of Oral Diseases: A Review on the Current Literature. *J. Or. H. Com. Den*. 15(2): 71 (2021).
DOI: 10.5005/jp-journals-10062-0085

43. Harfouch R. M., Darwish M., Ghosh S., Beesh M., Ibrahem N., Dayoub H., Zein R., Ahamadi S.: Formulation and Preparation of a Novel Toothpaste Using the Essential Oil of Salvia officinalis. 2021: 3770309 (2021).
DOI: 10.2139/ssrn.3770309

44. Milenković M. T., Božić D. D., Slavkovska V. N., Lakušić B. S.: Synergistic effects of *Salvia officinalis* L. essential oils and antibiotics against methicillin-resistant Staphylococcus aureus. *Arch. Bio. Sci*. 67(3): 949-56 (2015).
DOI: 10.2298/abs141119057m

45. Fournomiti M., Kimbaris A., Mantzourani I., Plessas S., Theodoridou I., Papaemmanouil V., Kapsiotis I., Panopoulou M., Stavropoulou E., Bezirtzoglou E. E., Alexopoulos A.: Antimicrobial activity of essential oils of cultivated oregano (*Origanum vulgare*), sage (*Salvia officinalis*), and thyme (*Thymus vulgaris*) against clinical isolates of *Escherichia coli*, *Klebsiella oxytoca*, and *Klebsiella pneumoniae*. *Micr. Eco. H. Dis*. 26(1): 23289 (2015).
DOI: 10.3402/mehd.v26.23289

46. Mendes F. S., Garcia L. M., da Silva Moraes T., Casemiro L. A., de Alcantara C. B., Ambrósio S. R., Veneziani R. C., Miranda M. L., Martins C. H.: Antibacterial activity of *salvia officinalis* L. against periodontopathogens: An *in vitro* study. *Anaer.J.* 63: 102194 (2020).
DOI: 10.1016/j.anaerobe.2020.102194